

The Human Genome Epidemiology Network (HuGE Net)

Muin J. Khoury, MD, Ph.D.

**Director,
CDC Office of Genomics and Disease Prevention**

"Welcome to the Genomics Era"

(NEJM Dec 2003)

"Genetic Testing for Sale"

Vineis, P, Christiani, D. Epidemiology Jan 2004

The screenshot shows a Microsoft Internet Explorer browser window displaying the Genovations website. The browser's address bar shows the URL <http://www.genovations.com>. The website's header features the Genovations logo with the tagline "Predictive Genomics for Personalized Medicine". A sidebar on the left lists navigation options: Overview, For Patients, For Clinicians, Lab Tests, Education, and Resources. The main content area includes a headline stating "Genovations™ is the advent of truly personalized healthcare." followed by a paragraph about harnessing genomic science for preventive biomedicine. Below this, a list of benefits is provided: earlier preventive interventions, precise customized therapies, and improved clinical insight. A "LATEST NEWS" section on the right lists a press release, a CNBC/Health Network feature, and a sign-up link. At the bottom of the main content area, there is a photograph of Genovations product boxes and a red card. The Windows taskbar at the bottom shows the Start button and several open applications, including Internet Explorer, Ideas for Genomics, Corel WordPerfect, and Microsoft PowerPoint. The system clock indicates 8:16 PM.

Genovations- Predictive Genomics - Microsoft Internet Explorer

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Address <http://www.genovations.com> Home Go

Links Customize Links Free Hotmail RealPlayer Windows Windows Media Get \$\$\$ - Refer a friend!

GENOVATIONS™

Predictive Genomics for Personalized Medicine

Great Smokies Diagnostic Laboratory

Overview
For Patients
For Clinicians
Lab Tests
Education
Resources

Genovations™ is the advent of truly personalized healthcare.

By harnessing the ingenuity of new breakthroughs in genomic science with the power of preventive biomedicine, Genovations™ offers an innovative, advanced health care model for more effectively preventing and treating chronic disease.

Our predictive genomic profiles assess genetic variations in each person that, when combined with modifiable factors in the environment, may increase disease risk. This empowers physicians and patients to realize:

- Earlier, more effective preventive interventions—years before disease develops
- Precise, customized therapies that truly address each individual's needs
- Improved clinical insight into patients with treatment-resistant "chronic" conditions

LATEST NEWS

- ▶ [Press Release](#)
- ▶ [CNBC/Health Network feature](#)
- ▶ [Sign Up for More](#)

GENOVATIONS

Internet

start 3 Internet Explorer Ideas for Genomics ... Corel WordPerfect ... Microsoft PowerPoin... My Computer 8:16 PM

"Welcome to the Genomics Era"

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DNA Direct | Genetic Tests - Microsoft Internet Explorer

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Address <http://www.dnadirect.com/> Go Links

DNAdirect

Your Genes In Context

Home Why Test Why Direct Genetic Tests Services Resources About Us

Register | Login

Personalized Genetic Testing

Your genes.
Your health.
Your choices.

- 1. DECIDE**
if genetic testing is right for you
- 2. ORDER**
a test online through DNA Direct
- 3. DISCOVER**
the results from your Personal Report

"Information is power... [testing] was not something that came from an edict from my insurance company or my doctor. It came from my own curiosity about my body and my health.... And for me, having more information is better."

— Andrew Zolli, [Marketplace](#) on National Public Radio

Benefits of Testing

Some genetic conditions can be prevented or treated.

Private Test Results

Our tests are quality-assured and completely confidential.

What You'll Learn

Learn practical steps to improve your health. Get info for your doctors and

How It Works

Testing is as easy as 1-2-3. Walk through our easy home-test process.

Done Internet

Start Disco... Inbo... Micro... RE: ... DNA ... 9:54 AM

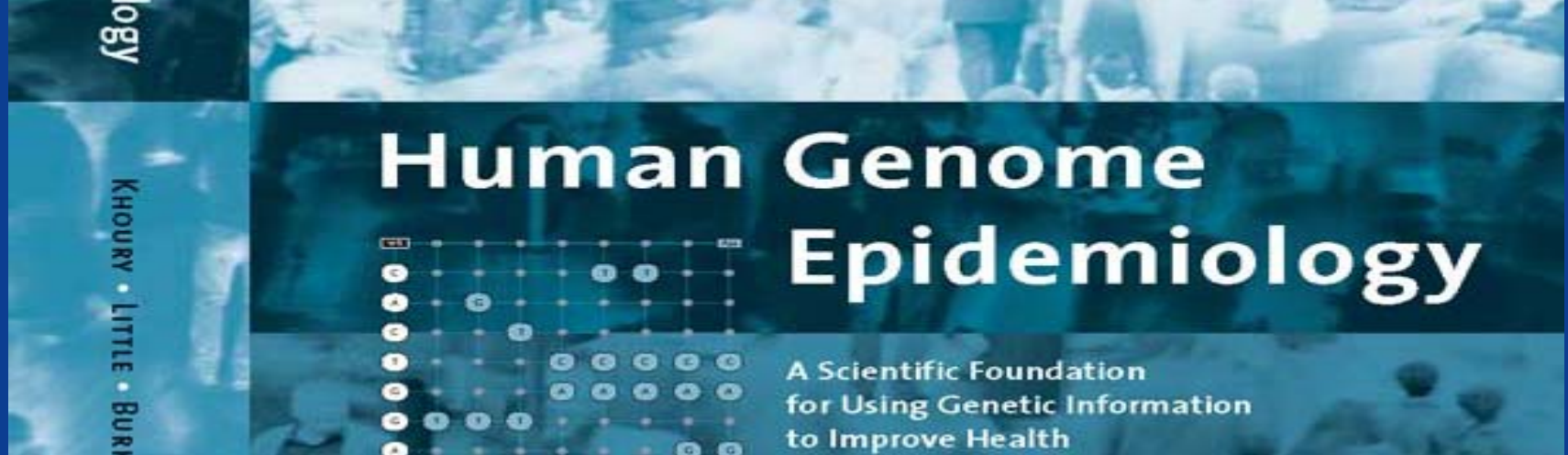
Gene-Based Medicine in 2010?

“Hypothetical Genetic Test Report”

• Condition	Genes	RR	Lifetime
• Prostate Ca	HPC1, 2, 3	0.4	7%
• Alzheimer's	APOE,FAD3,XAD	0.3	10%
• Heart disease	APOB,CETP	2.5	70%
• Colon Cancer	FCC4,APC	4.0	23%
• Lung Cancer	NAT2	6.0	40%

Collins FC, New Engl J Med 1999;341:28-37.

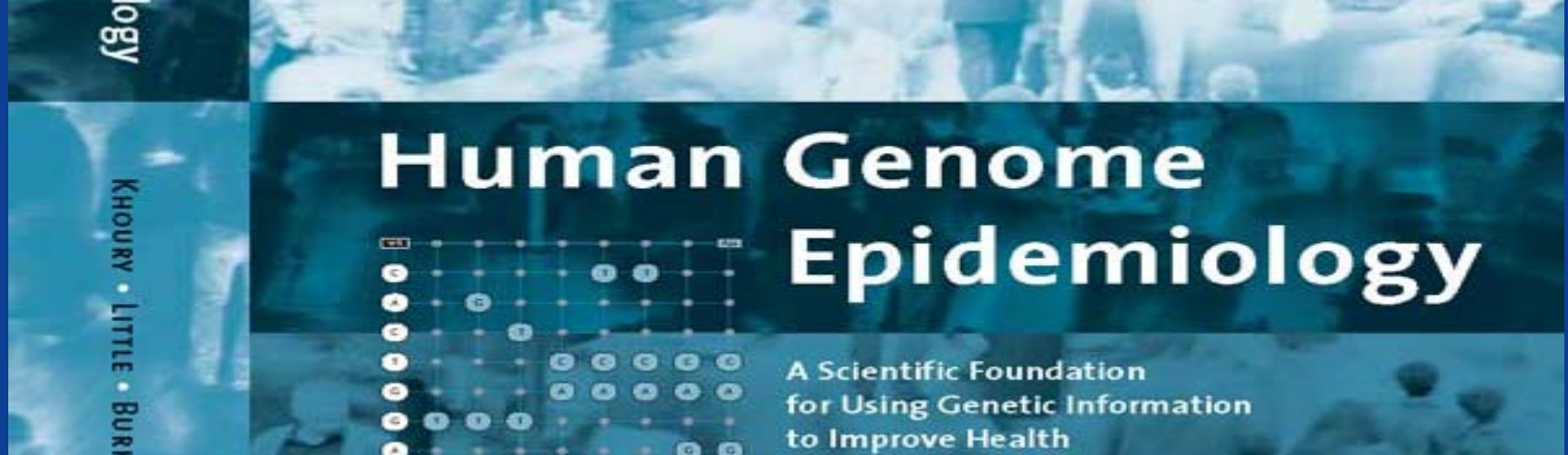




“Systematic application of epidemiologic methods and approaches to assess the impact of human genetic variation on health and disease”

Khoury, Little and Burke, HuGE 2004

- Genotype prevalence
- Gene - disease association
- Gene - gene interactions
- Gene - environment interactions
- Assessment of Genetic tests



“Systematic application of epidemiologic methods and approaches to assess the impact of human genetic variation on health and disease”

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- Gene - environment interactions
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HuGE problem:
25,000 genes, their combinations and interactions with risk factors

The End of Black Box Epidemiology?

Risk Factors

Demographics

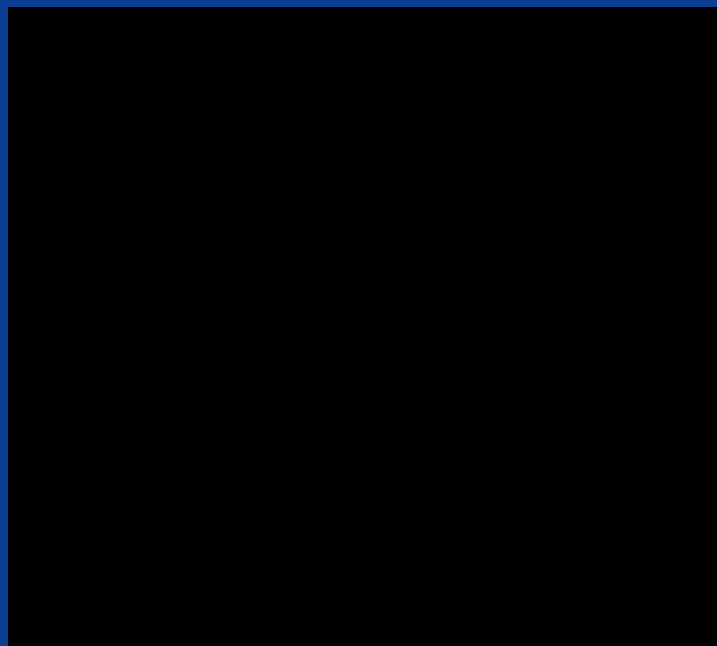
Diet

Occupation

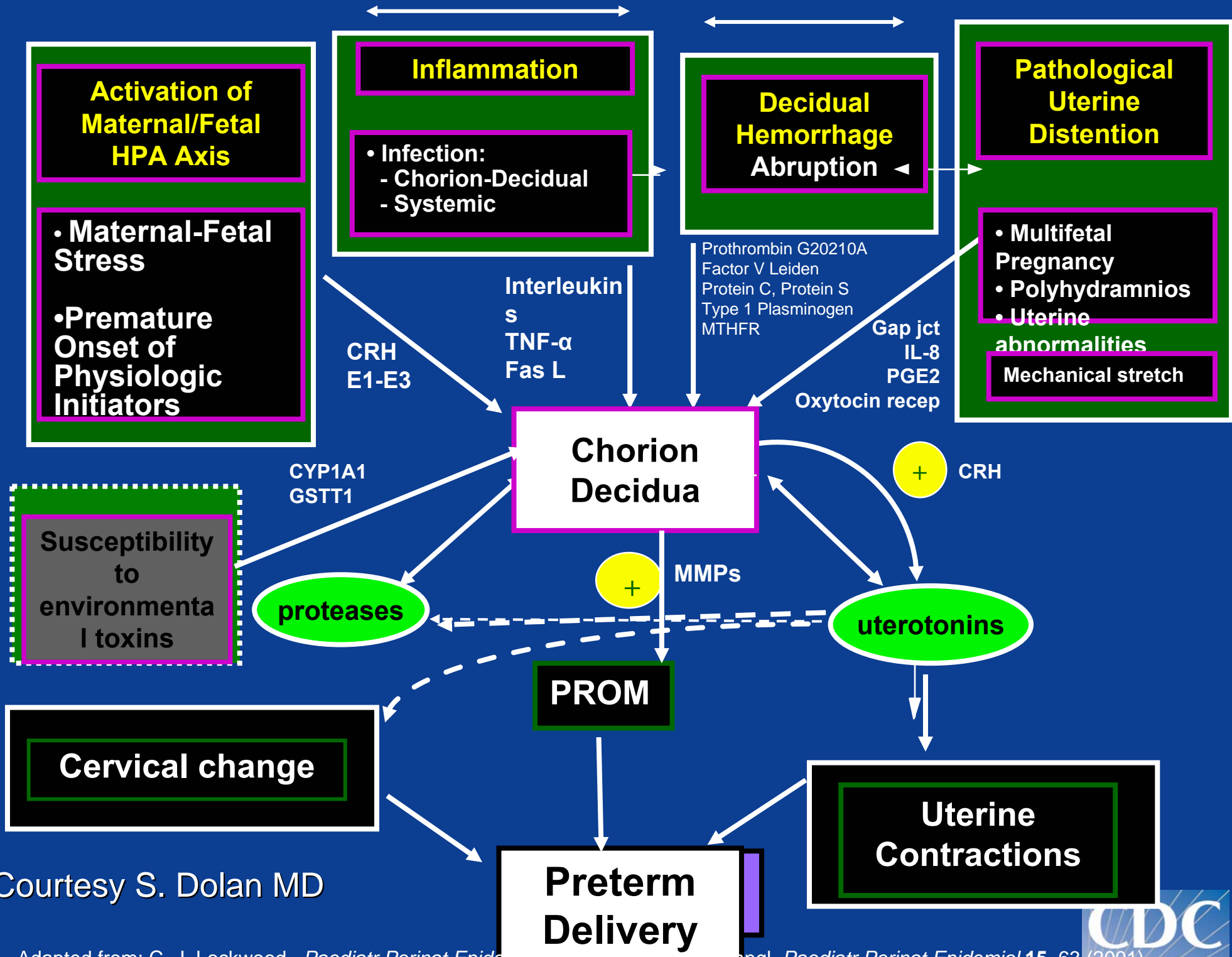
Smoking

Alcohol

Environment



**Adverse
Health
Outcomes**



Courtesy S. Dolan MD

From HuGE Research to Synthesis & Dissemination for Policy and Practice

Primary HuGE Research
Agenda and Funding

Study Design
Single studies
(case-control,
cohort
biobanks)
Consortia

Implementation

Candidate gene selection
Risk factor data
Outcome data

Identify

Knowledge gaps
Methodologic
problems
Research Priorities

Analysis: G-G, G-E

Interpretation

Causal inference
Risk estimation

Dissemination

Appraisal
(Single study)

Synthesis

Reviews
Meta-analysis

**Policy &
Practice**

From HuGE Research to Synthesis & Dissemination for Policy and Practice

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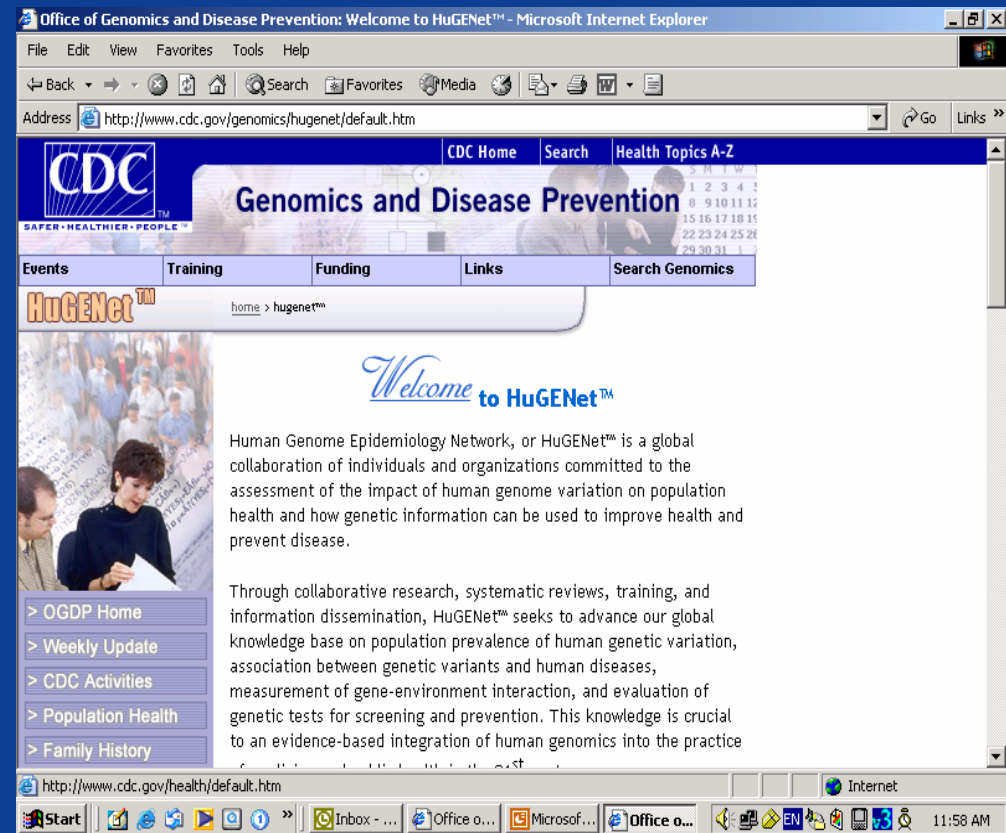
Synthesis

Reviews
Meta-analysis

**Policy &
Practice**

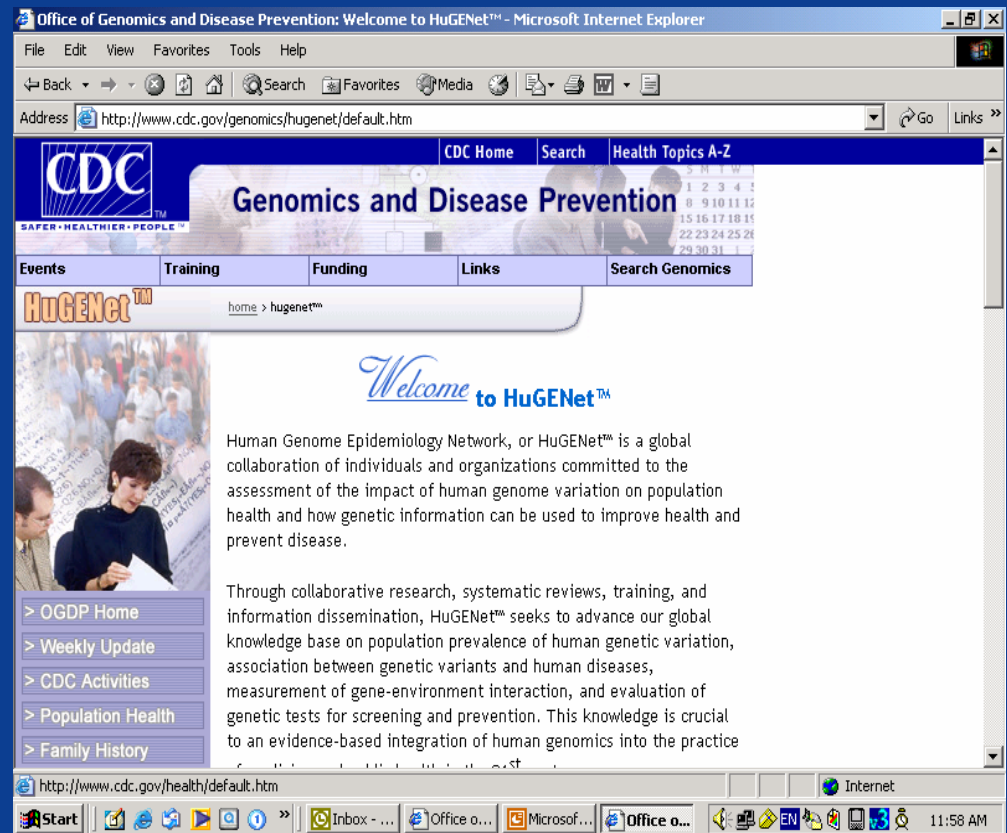
Human Genome Epidemiology Network (HuGE Net)

- Global collaboration of individuals and organizations to assess population impact of genomics and how it can be used to improve health and prevent disease (~700 collaborators, 43 countries)



Human Genome Epidemiology Network (HuGE Net)

- Information Exchange
- Training and Technical Assistance
- Knowledge Base Development
- Information Dissemination
- Policy Development



From HuGE Research to Synthesis & Dissemination for Policy and Practice

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cohort
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(Single study)

Synthesis

HuGE
Meta-analysis

**Policy &
Practice**

HuGE Net Products

(as of January 10, 2005)

- **Reviews** 33
- **Fact sheets** 13
- **E-journal clubs** 53
- **Case studies** 4
- **Genotype Prevalence Database** 13
- **Methods workshop/guidelines** 2
- **Training workshops** 6
- **Book** 1

- **Published Literature Database** 14,127
 - **# Genes** 1710
 - **# Risk Factors** 559
 - **# Outcomes** 1797

HuGE Reviews

“Systematic Reviews of Gene-Disease Associations”

- Full Reviews
 - Abstract
 - Gene
 - Gene variants Prevalence
 - Disease/Health outcome
 - Associations
 - Interactions
 - Laboratory Tests
 - Population Testing and other applications
 - Recommendations for further research
- Mini-Reviews
- Gene-Disease Association Reviews
- Prevalence Reviews



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HUMAN GENOME EPIDEMIOLOGY (HuGE) REVIEW

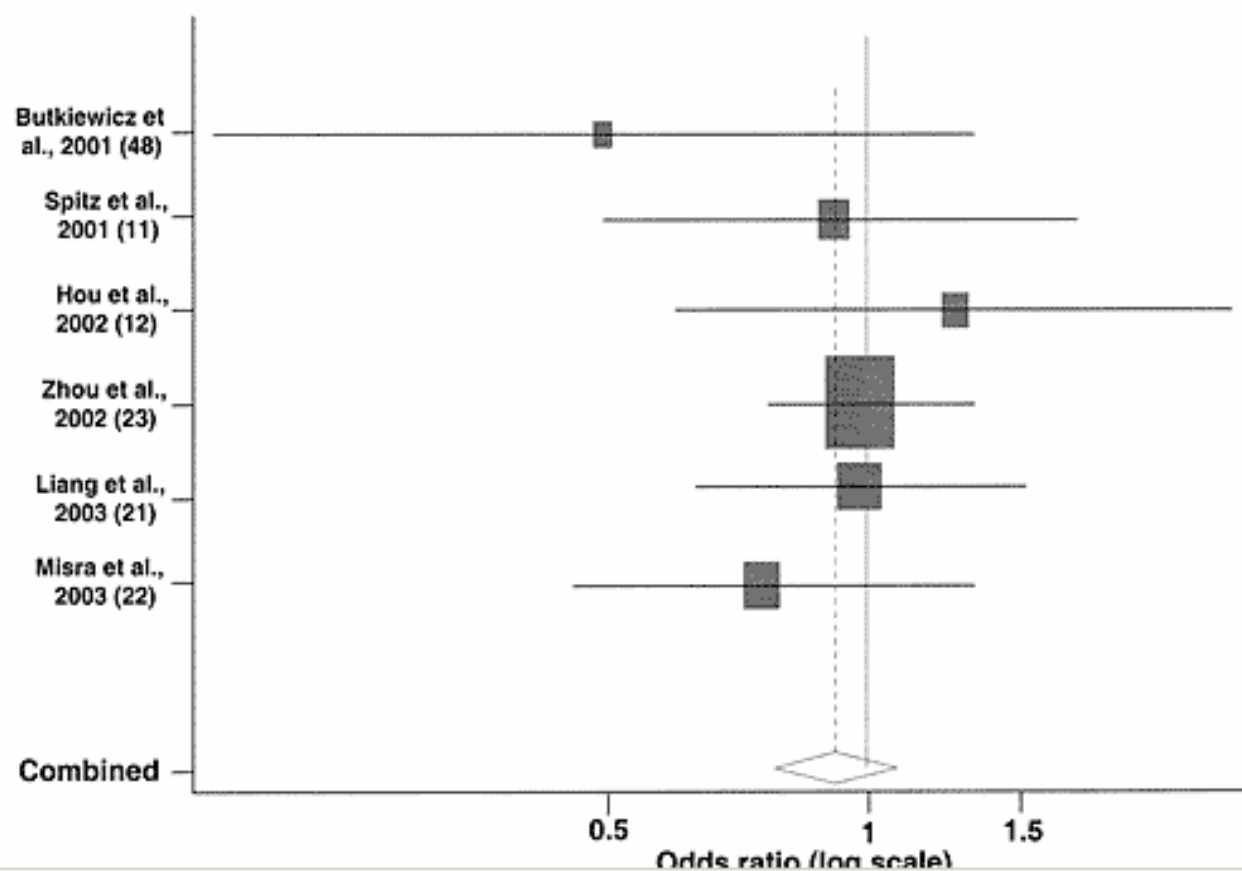
ERCC2/XPD Gene Polymorphisms and Lung Cancer: A HuGE Review

Simone Benhamou^{1,2} and Alain Sarasin²

8.1 x 10.88 in

1 of 14

Figure 2: Odds ratios for the relation between the *Asp / Asn* genotype of the xeroderma pigmentosum group D *Asp 312 Asn* gene polymorphism (vs. the *Asp / Asp* genotype) and lung cancer risk. For each study, the odds ratio estimate is plotted with a box; the area of each box is inversely proportional to the estimated effect's variance in the study. Diamond, pooled odds ratio; horizontal lines, 95% confidence interval.



HuGE Reviews by Topic

Jan 10, 2005

- Cancer 13
- Cardiovascular 4
- Birth Defects 4
- Single Gene Ds 4
- Exposures 3
- Others 5

Systematic Reviews of Gene-Disease Associations: GDP Info: Oct 2000-Aug 2004

Category	Number	%
Cancer	34	23.9
Cardiovascular diseases	27	19.0
Mental Health	25	17.6
Neurologic diseases	12	8.5
Osteoporosis	6	4.2
Pregnancy/Reproduction	5	3.5
Infectious diseases (all HIV)	4	2.8
Diabetes	3	2.1
Autoimmune diseases	3	2.1
Obesity	2	1.4
Arthritis	2	1.4
Asthma	2	1.4



Genomics and Disease Prevention Information System (GDPIInfo)

GDPIInfo is a searchable database of documents available on the Office of Genomics and Disease Prevention's (OGDP) Web site as well as links to relevant documents on other sites.

Try it! Search by

Gene

Disease

Interactive Factor



What is in GDPIInfo?

- fact sheets
- reviews
- case studies
- published literature
- online presentations
- books and book chapters
- materials from conferences and workshops

Why GDPIInfo?

To provide access to information and resources for guiding public health research, policy, and practice on using genetic information to improve health and prevent disease.

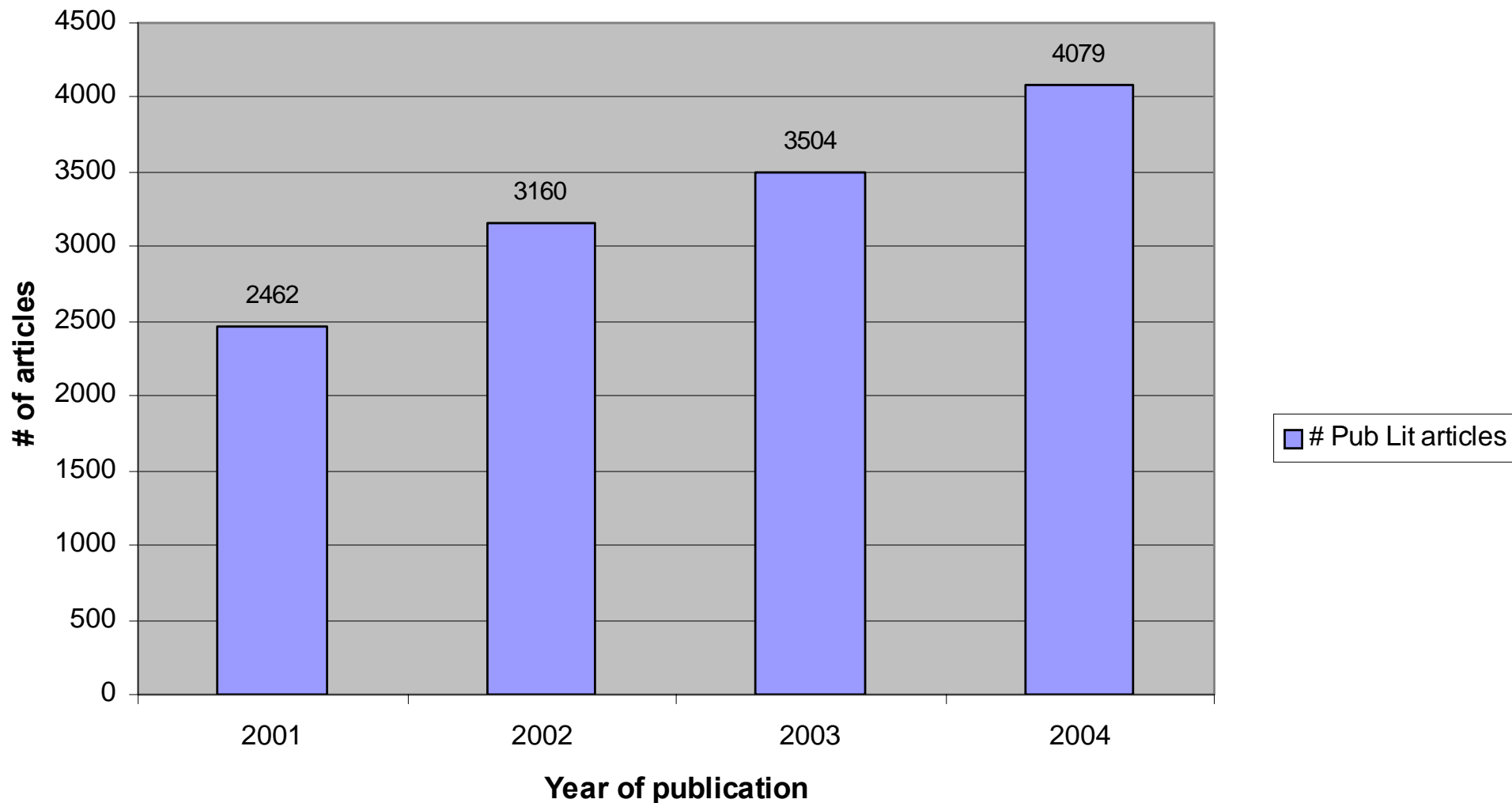
Who Uses GDPIInfo?

Public health professionals are the target audience but there are data and information for researchers, health care providers, and the general public.

<http://www.cdc.gov/genomics>



No. of articles in Huge Published Literature db, 2001-2004*



(*As of Jan 14, 2005. Count excludes review articles, meta & pooled analyses.)

Number of Published HuGE Papers* 2001-2004

• Year	Prevalence	Associations	Interactions
• 2001	308	2141	436
• 2002	349	2799	569
• 2003	323	3010	598
• 2004	368	3486	604

* Data from CDC's GDP Info 1/2005



Search

The last time you searched you selected a combination of genes, diseases/conditions, topics and other factors.

[Basic Search](#) | [Advanced Search](#) | [Search Instructions](#) | [Home](#) | [About GDPInfo](#) | [Contact Us](#)**Genes: Enter a gene(s) or select an item from the Gene Menu.**

Gene(s)

[Search gene through GDB](#)

Gene Menu

Current Selected Gene(s)

MTHFR

Indicate "And" or "Or" if more than one gene.

Or

Disease/Conditions: Enter a disease/condition or select an item from the Disease Menu.

Disease(s)

Disease/Condition Menu

Current Selected Disease(s)

Indicate "And" or "Or" if more than one disease.

Or

Environmental or Personal Factors: Enter a Factor or select an item from the Factor Menu.

Factor(s)

Factor Menu

Current Selected Factor(s)

Indicate "And" or "Or" if more than one factor.

Or

[New Search](#)

You have selected one or more choices below.

Gene(s): MTHFR

And

Factor(s):

And

Disease/Condition(s):

Search Result Sort By ☒ Title ☐ Year Published

Expand	Document Source	Record(s) Found
	HuGE E-Journal	4
	Fact Sheet	1
	Genotype Prevalence Table	Expand for details
	HuGE Published Literature	602
	HuGE Review	3
	Online Presentation	1
	Other Reports and Publications	6

[New Search](#)

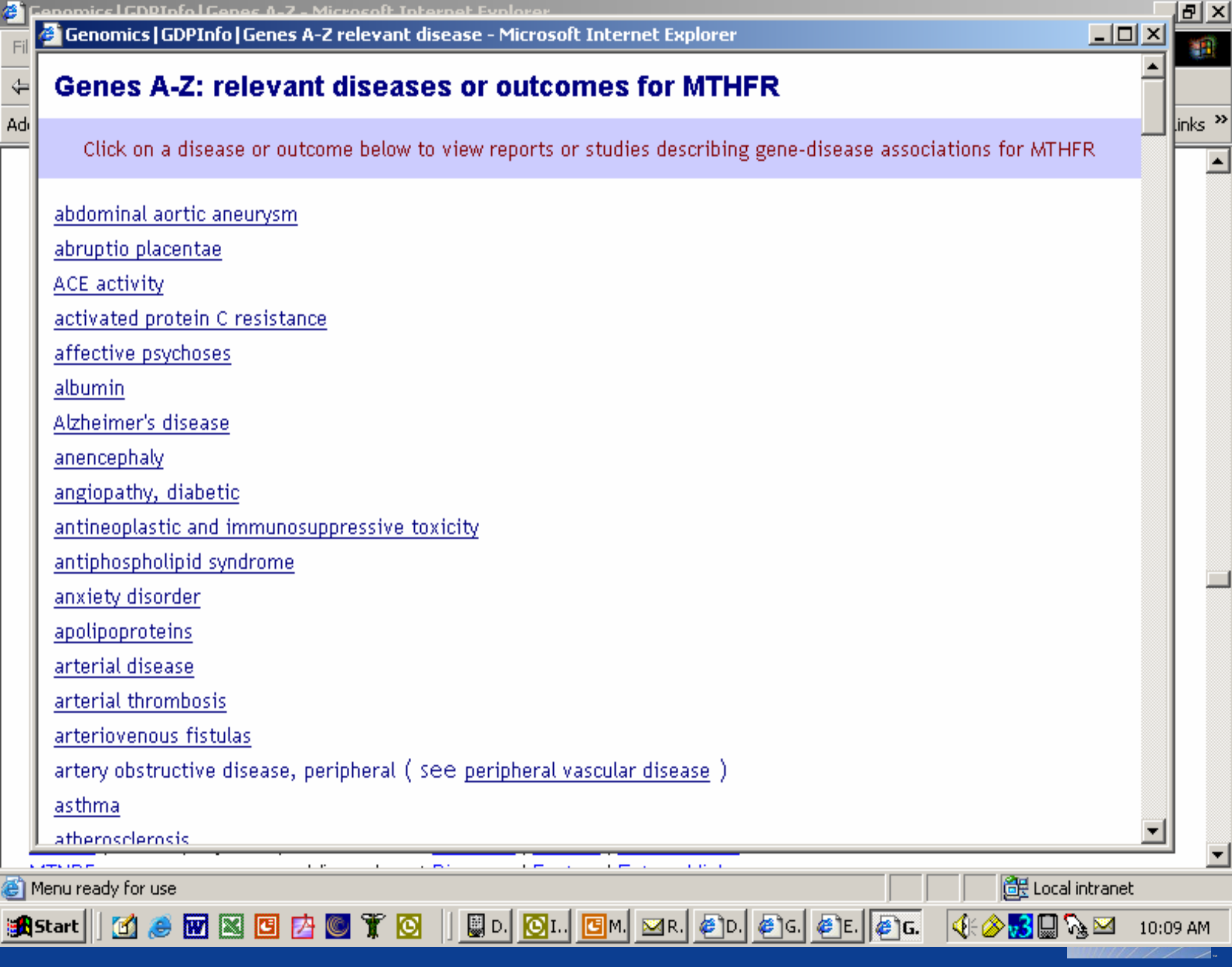
This application is best viewed in Microsoft Internet Explorer 5 or greater or in Netscape 6 or greater.

Gene: MTHFR (5,10-methylenetetrahydrofolate reductase (NADPH))

Click on a column to sort data

View: ☒ Prevalence (%) ☐ 95% Confidence

<u>Study Location (Reference #)</u>	<u>Gender</u>	<u>Race Or Ethnicity</u>	<u># Subjects Studied</u>	<u>g.677C>T/g.677C>T</u>	<u>g.677C>T/g.677C</u>	<u>g.677C/g.677C</u>	<u>g.1298A>C/g.1298A>C</u>	<u>g.1298A>C/g.1298</u>
Africa (#41)	NS	African, sub-Saharan	234	0	13.2	86.8	-1	-1
Zaire & Cameroon (#42)	NS	NS	67	0	10.4	89.6	-1	-1
South Africa (#75)	NS	Black	114	-1	-1	-1	4.4	34.2
Asia (#41)	NS	Asian	346	3.5	28.3	68.2	-1	-1
Japan (#45)	M	Japanese	129	10.9	54.3	34.9	-1	-1
Japan (#46)	NS	NS	419	12.2	51.1	36.8	-1	-1
Japan (#47)	M	NS	778	10.2	46.4	43.4	-1	-1
Japan (#48)	M	Japanese	325	10.2	42.8	47.1	-1	-1
Japan (#49)	F	NS	98	11.2	50	38.8	-1	-1
Japan (#50)	NS	NS	260	11.2	51.9	36.9	-1	-1
Japan (#51)	NS	NS	105	18.1	48.6	33.3	-1	-1
Japan (#52)	NS	NS	310	13.5	51	35.5	-1	-1
Japan (#53)	NS	NS	146	11.6	29.5	58.9	-1	-1
Japan (#78)	NS	NS	243	-1	-1	-1	3.7	30.9



Genes A-Z: relevant diseases or outcomes for MTHFR

Click on a disease or outcome below to view reports or studies describing gene-disease associations for MTHFR

[abdominal aortic aneurysm](#)

[abruptio placentae](#)

[ACE activity](#)

[activated protein C resistance](#)

[affective psychoses](#)

[albumin](#)

[Alzheimer's disease](#)

[anencephaly](#)

[angiopathy, diabetic](#)

[antineoplastic and immunosuppressive toxicity](#)

[antiphospholipid syndrome](#)

[anxiety disorder](#)

[apolipoproteins](#)

[arterial disease](#)

[arterial thrombosis](#)

[arteriovenous fistulas](#)

[artery obstructive disease, peripheral \(see \[peripheral vascular disease\]\(#\) \)](#)

[asthma](#)

[atherosclerosis](#)

Gene Menu

MTHFR


Or

Disease/Condition Menu

*ALL (Congenital anomalies)

Or

Factor Menu


Or 

Genomics | GDPInfo | Search result - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Home Search Favorites Media

Address http://www2a.cdc.gov/genomics/GDPQueryTool/frmQuerySumPage.asp?IO_strGeneSymbol=&IO_strGeneSymbolValue=MTHFR Go Links



The GDPInfo query tool allows you to define your search with a combination of genes, diseases/conditions, topics and other factors.

New Search

You have selected one or more choices below.




Gene(s): MTHFR

And Factor(s):

And Disease/Condition(s): *ALL (Congenital anomalies)

Search Result

Sort By ☒ Title ☐ Year Published


Expand	Document Source	Record(s) Found
	HuGE Published Literature	45
	HuGE Review	1
	Other Reports and Publications	3


New Search

Done

Local intranet

Start



 8:15 AM

[CDC Home](#)[Search](#)[Health Topics A-Z](#)

Genomics and Disease Prevention

[Events](#)[Training](#)[Funding](#)[Links](#)[Search Genomics](#)**HuGE Review**[home](#) > [hugenet](#) > [reviews](#) > [MTHFR gene and congenital anomalies](#)

This paper was published with modifications in *Am J Epidemiol* 2000 May 1;151(9):862-877

PMID: 10791559; UI: 20250198

5, 10-Methylenetetrahydrofolate reductase (*MTHFR*) Gene Variants and Congenital Anomalies

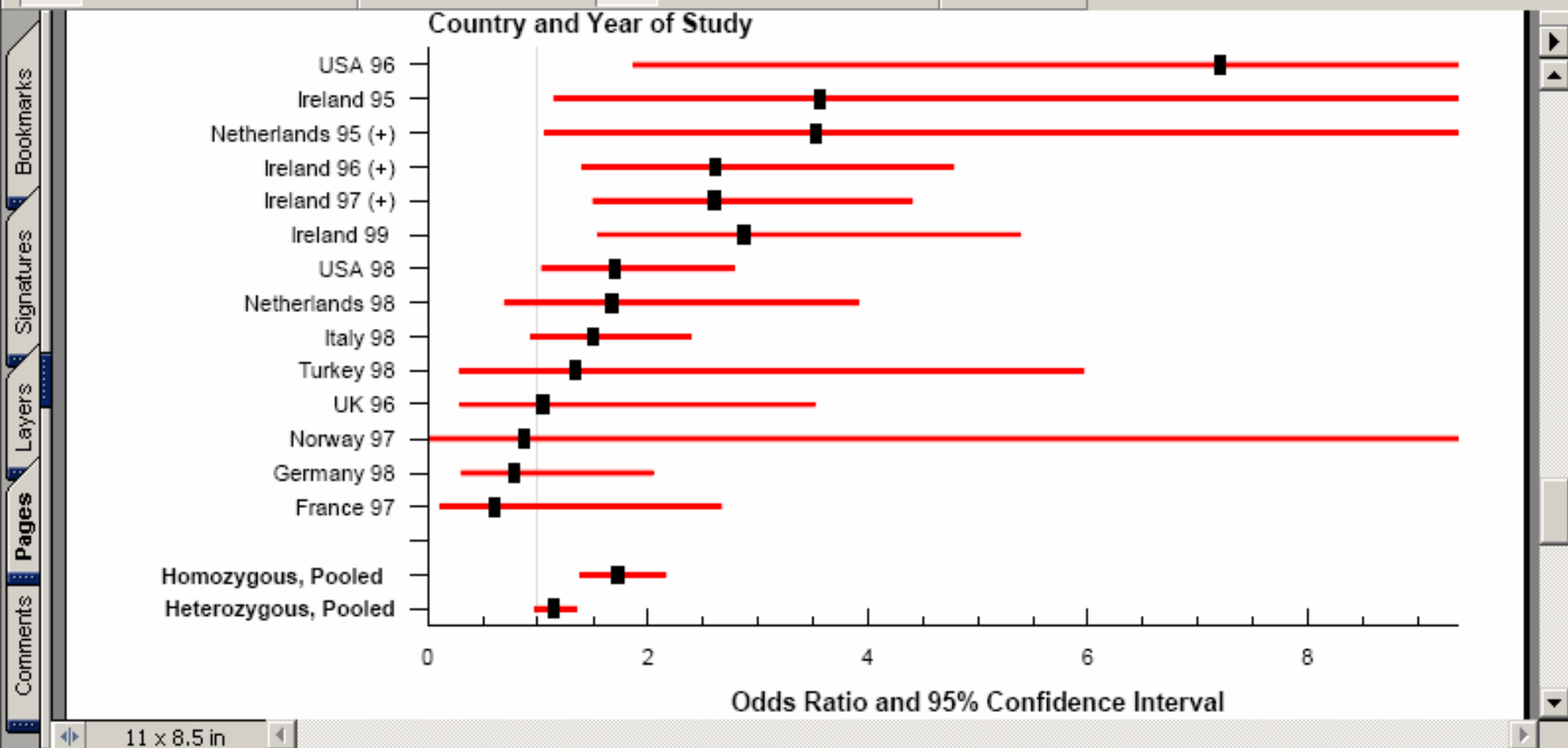
Lorenzo D. Botto and Quanhe Yang

[Download print version](#)

Authors' affiliations:

Centers for Disease Control and Prevention, National Center for Environmental Health, Division of Birth Defects and Pediatric Genetics, Atlanta, GA

August 16, 2000



HuGE Net Next Steps

- Knowledge base development
 - Develop tools for synthesis (“Cochrane” manual)
 - Develop research agenda and Pilot projects
- Enhance collaborations and information Sharing
 - “Network of Networks”
 - **Collaboration with Biobanks**
- Training and technical assistance
- Electronic journal (forum for negative studies)
- Use in public health genetics policy and practice

From HuGE Research to Synthesis & Dissemination for Policy and Practice

